REMARKS/ARGUMENTS

Claims 1, 3, 5-9, and 12-19 have been pending in the above-captioned application. Claims 8, 9 and 13-17 have earlier been withdrawn from consideration. Claim 1 has now been amended to more particularly point out and distinctly claim that which Applicants consider to be their invention. As a result of this amendment claim 18 has been cancelled.

Upon entry of the above-made amendments, therefore claims 1, 3, 5-9, 11-17, 19 will be pending in the current application. The amended claims are fully supported in the specification as originally filed. The amendments to the Claims do not add new matter. Applicants respectively request that the amendments be entered.

The following remarks, in conjunction with the above amendments, are believed to be fully responsive to the Office Action.

THE REJECTION UNDER 35 U.S.C. § 102 SHOULD BE WITHDRAWN

Claims 1, 3, 5-7, 11-12, 18-19 are rejected under 35 U.S.C. 102(b) as being anticipated by Unger US Patent 6,033,645. In response, Applicants submit that the rejection should be withdrawn for the reasons stated below.

As noted above, claim 1 has been amended to recite that the invention is directed to administration of a gas-containing contrast agent by continuous infusion over an infusion period of 5-60 minutes, wherein the contrast agent is delivered from the upper extremity of an essentially vertically positioned syringe. A basis for the amendment, specifying the period of administration of the contrast agent, is found on page 15, examples 1-6. These examples all show that the contrast agent should be administered during the period of steady state, i.e. over a period of 5-60 minutes.

A finding of anticipation under 35 U.S.C. 102 requires the disclosure in a single prior art reference of each element of the claim under consideration. *W.L. Gore & Associates v. Garlock, Inc.*, 721 F.2d 1540, 220 USPQ 303 (Fed. Cir. 1983). There must be no difference between the claimed invention and the reference disclosure, as viewed by a person of ordinary skill in the field of the invention. *Scripps Clinic & Research Found. v. Genetech Inc.*, 927 F.2d 1565, 18 USPQ 2d 1001, 1010 (Fed. Cir. 1991).

The present invention is drawn to administration of a gas-containing contrast agent by continuous infusion. The contrast agent is delivered from an upper extremity of an essentially vertically positioned delivery vessel, and is admixed with a flushing medium prior to administration to a subject. The present invention has identified a solution to the problem of administering a gas-containing contrast agent by infusion. Infusion is normally defined as the continuous intravenous administration of an agent over a sufficiently long time period to obtain a steady state level of the agent in blood. A problem with the continuous infusion of gas-containing diagnostic contrast agents arises from the tendency of gas-containing components to float, since this will lead to inhomogenities forming within vessels such as power-driven syringes which may be used to administer the contrast agent. This may, for example, lead to an increase in microbubble concentration in the upper part of such a vessel and/or to changes in size distribution occurring at various points within the vessel as larger microbubbles float more rapidly than smaller microbubbles. This problem increases with increased time of administration of the contrast agent. By combining delivering from the top of a vertically positioned syringe and admixing with a flush medium prior to administration to a patient, the segregation is minimized and enhanced product homogeneity is achieved. By using a syringe as the delivery reservoir and placing this in a vertical position, with the outlet pointing upwards, the effects of floatation separation is greatly reduced, as further explained in the specification on page 3 and 4. The admixing with a flushing medium further enhances the homogeneity of the contrast agent that is delivered to the patient, e.g. by reducing the residence time of the agent in connecting tubes etc. It is further preferred that the syringe is positioned so that the bulk flow direction of the gas-containing contrast agent during expulsion is the same as the direction of segregation of the dispersed gas-bubble

phase, i.e. upwards, since this will assist in counteracting the formation of concentration gradients of the dispersed gas-bubbles during administration.

Unger discloses ultrasound contrast agents and delivery of such to a patient. However, as outlined in our previous response Unger fails to teach admixing of the contrast agent with a flushing agent over time. He also fails to teach administration by continuous infusion, i.e. non-interrupted administration of the contrast agent and simultaneous admixture with flushing medium over time. Unger describes that diagnostic artifacts such as shadowing may be reduced by controlling the rate of administration of the contrast agent and/or by administering a flush such as normal saline after administration of the contrast agent. The contrast agent of Unger is typically administered over a period of 5 seconds (column 45, line 20), or up to a period of 50 seconds ((column 3, line 55), and any subsequent flush is typically administered over a period in the range 10 seconds to 10 minutes. Unger suggests that the rate of administration of the contrast agent relate to the occurrence of diagnostic artifacts. To promote the transport of the contrast agent from the injection site into the bloodstream, a flush may be administered to push or wash the contrast agent into the bloodstream (page 70). The contrast agent is hence delivered over a very short period, while the flushing media may be administered over a longer period. When Unger refers to "continuous infusion" in claims 1 and 209, the Applicant interprets this to mean administration of the flushing medium over a longer period, and not of the contrast agent. With regard to avoiding artifacts in the image his solution lies in speed of the flushing medium.

The present invention, however, has identified a solution to the problem of administering a gas-containing contrast agent over long period, i.e. an infusion period of 5-60 minutes a period, necessary to obtain steady state of the contrast agent in the blood. Unger does not teach the administration of a gas-containing contrast agent over a period of 5-60 minutes and hence does not teach each element of the claim under consideration, i.e. the amended claim 1.

Thus, Applicants respectfully submit that the Examiner's rejection under 35 U.S.C. 102 (b) has been overcome and/or obviated and respectfully request that the rejections be withdrawn.

CONCLUSIONS

In view of the amendments and remarks herein, Applicants believe that each ground for rejection or objection made in the instant application has been successfully overcome or obviated, and that all the pending claims are in condition for allowance. Withdrawal of the Examiner's rejections and objections, and allowance of the current application are respectfully requested.

The Examiner is invited to telephone the undersigned in order to resolve any issues that might arise and to promote the efficient examination of the current application.

Respectfully submitted,

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